Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSSPTA1626GMS

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
Welcome to STN International
NEWS 1
                 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2
                 "Ask CAS" for self-help around the clock
NEWS 3 JAN 17
                 Pre-1988 INPI data added to MARPAT
NEWS 4 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist
                 visualization results
NEWS 5 FEB 22 The IPC thesaurus added to additional patent databases on STN
NEWS 6 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 7 FEB 27
                New STN AnaVist pricing effective March 1, 2006
NEWS 8 MAR 03
                Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 9 MAR 22
                 EMBASE is now updated on a daily basis
NEWS 10 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 11 APR 03
                 Bibliographic data updates resume; new IPC 8 fields and IPC
                 thesaurus added in PCTFULL
NEWS 12
        APR 04
                 STN AnaVist $500 visualization usage credit offered
NEWS 13
        APR 12
                LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 14
        APR 12
                 Improved structure highlighting in FQHIT and QHIT display
                 in MARPAT
NEWS 15
        APR 12
                Derwent World Patents Index to be reloaded and enhanced during
                 second quarter; strategies may be affected
NEWS 16 MAY 10
                CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 17 MAY 11
                KOREAPAT updates resume
NEWS 18 MAY 19
                Derwent World Patents Index to be reloaded and enhanced
NEWS 19 MAY 30
                IPC 8 Rolled-up Core codes added to CA/CAplus and
                 USPATFULL/USPAT2
NEWS 20 MAY 30
                The F-Term thesaurus is now available in CA/CAplus
NEWS 21
        JUN 02
                The first reclassification of IPC codes now complete in
                 INPADOC
NEWS EXPRESS
                 FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
                 CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
                AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
                V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
                http://download.cas.org/express/v8.0-Discover/
             STN Operating Hours Plus Help Desk Availability
NEWS HOURS
```

Enter NEWS followed by the item number or name to see news on that specific topic.

Welcome Banner and News Items

All use of STN is subject to the provisions of the STN Customer

NEWS LOGIN NEWS IPC8

NEWS X25

For general information regarding STN implementation of IPC 8

X.25 communication option no longer available after June 2006

agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 14:41:12 ON 09 JUN 2006

=> Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE Do you want to switch to the Registry File? Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 14:41:24 ON 09 JUN 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 JUN 2006 HIGHEST RN 887296-19-7 DICTIONARY FILE UPDATES: 8 JUN 2006 HIGHEST RN 887296-19-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information

on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>

Uploading C:\Program Files\Stnexp\Queries\10814410.str

chain nodes :

12 13 14 15 16 17 18 19 20 21 23

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :

2-13 5-17 9-15 10-12 12-13 12-16 13-14 17-18 18-19 19-20 20-21 20-23

ring bonds :

1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11

exact/norm bonds :

9-15 10-12 12-13 13-14 17-18 18-19 19-20 20-23

exact bonds :

1-2 1-5 2-3 2-13 3-4 4-5 5-17 12-16 20-21

normalized bonds :

6-7 6-11 7-8 8-9 9-10 10-11

isolated ring systems :

containing 1 : 6 :

G1:Cy, Hy, Ph

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS 21:CLASS 23:CLASS

## L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 14:41:42 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED

0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

O TO

PROJECTED ANSWERS:

0 TO

0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 14:41:48 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 34 TO ITERATE

100.0% PROCESSED

34 ITERATIONS

16 ANSWERS

SEARCH TIME: 00.00.01

L3

L2

16 SEA SSS FUL L1

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY SESSION 167.15

166.94

FILE 'HCAPLUS' ENTERED AT 14:41:53 ON 09 JUN 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is

10814410.trn

Page 4

held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 9 Jun 2006 VOL 144 ISS 25 FILE LAST UPDATED: 8 Jun 2006 (20060608/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13 L4

1 L3

=> FIL REGISTRY
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 2.53 169.68

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 14:42:42 ON 09 JUN 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 JUN 2006 HIGHEST RN 887296-19-7 DICTIONARY FILE UPDATES: 8 JUN 2006 HIGHEST RN 887296-19-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

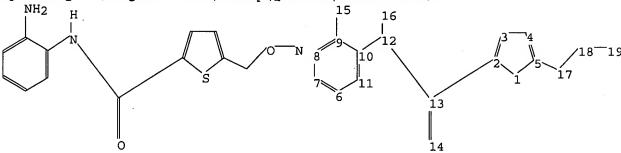
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> Uploading C:\Program Files\Stnexp\Queries\10814410a.str



chain nodes :

12 13 14 15 16 17 18 19

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :

2-13 5-17 9-15 10-12 12-13 12-16 13-14 17-18 18-19

ring bonds :

1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11

exact/norm bonds :

9-15 10-12 12-13 13-14 17-18 18-19

exact bonds :

1-2 1-5 2-3 2-13 3-4 4-5 5-17 12-16

normalized bonds :

6-7 6-11 7-8 8-9 9-10 10-11

isolated ring systems :

containing 1 : 6 :

G1:Cy, Hy, Ph

Match level

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS

L5 STRUCTURE UPLOADED

=> d 15

L5 HAS NO ANSWERS

L5 STR

G1 Cy,Hy,Ph

Structure attributes must be viewed using STN Express query preparation.

=> s 15

SAMPLE SEARCH INITIATED 14:43:00 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED

0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

0 TO 0

PROJECTED ANSWERS:

0 TO 0

L6

0 SEA SSS SAM L5

=> s 15 sss full

FULL SEARCH INITIATED 14:43:07 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -

36 TO ITERATE

100.0% PROCESSED

36 ITERATIONS

27 ANSWERS

SEARCH TIME: 00.00.01

L7

27 SEA SSS FUL L5

=>

Uploading C:\Program Files\Stnexp\Queries\10814410b.str

chain nodes :
12 13 14 15 16
ring nodes :
1 2 3 4 5 6 7 8 9 10 11
chain bonds :
2-13 9-15 10-12 12-13 12-16 13-14
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
9-15 10-12 12-13 13-14
exact bonds :
1-2 1-5 2-3 2-13 3-4 4-5 12-16
normalized bonds :
6-7 6-11 7-8 8-9 9-10 10-11
isolated ring systems :

G1:Cy, Hy, Ph

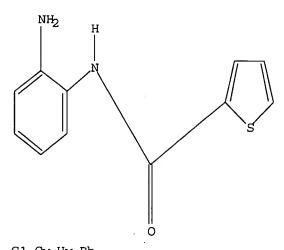
containing 1 : 6 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS

L8 STRUCTURE UPLOADED

=> d 18 L8 HAS NO ANSWERS L8 STR



G1 Cy, Hy, Ph

Structure attributes must be viewed using STN Express query preparation.

=> s 18

SAMPLE SEARCH INITIATED 14:44:18 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 108 TO ITERATE

100.0% PROCESSED

108 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

1537 TO 2783

PROJECTED ANSWERS:

8 TO 329

L9

8 SEA SSS SAM L8

=> s 18 sss full

FULL SEARCH INITIATED 14:44:24 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 2303 TO ITERATE

100.0% PROCESSED

2303 ITERATIONS

167 ANSWERS

SEARCH TIME: 00.00.01

L10

167 SEA SSS FUL L8

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE TOTAL

> ENTRY SESSION

FULL ESTIMATED COST 334.32 504.00

FILE 'HCAPLUS' ENTERED AT 14:44:28 ON 09 JUN 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is

10814410.trn

Page 9

held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 9 Jun 2006 VOL 144 ISS 25 FILE LAST UPDATED: 8 Jun 2006 (20060608/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 14:41:12 ON 09 JUN 2006)

FILE 'REGISTRY' ENTERED AT 14:41:24 ON 09 JUN 2006

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 16 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 14:41:53 ON 09 JUN 2006

L41 S L3

FILE 'REGISTRY' ENTERED AT 14:42:42 ON 09 JUN 2006

STRUCTURE UPLOADED

L6 0 S L5

L7 27 S L5 SSS FULL

L8 STRUCTURE UPLOADED

L9 8 S L8

L10 167 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 14:44:28 ON 09 JUN 2006

=> s 17

L5

L11 1 L7

=> s 110

L12 21 L10

=> d l4 ibib abs hitstr tot

ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:857590 HCAPLUS

DOCUMENT NUMBER:

141:332037

TITLE:

SOURCE:

Preparation of aminophenyl thiophenecarboxamide derivatives as HDAC inhibitors for the treatment of

wenter.

tumor growth

Fertig, Georg; Herting, Frank; Kubbies, Manfred; Limbers, Anja; Reiff, Ulrike; Weidner, Michael

Hoffmann-La Roche Ag, Switz.

PATENT ASSIGNEE(S): Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

10814410.trn

INVENTOR (S):

Page 10

LANGUAGE:

GI

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.					KIND DATE					APPLICATION NO.						DATE			
WO 2004087693								WO 2004-EP3498					20040402						
***																			
	w:										BG,								
											EC,								
																	LC,	•	
											MK,								
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,		
		TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZŅ		
	RW:										SZ,								
											BG,								
		ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI.		
		SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GO.	GW.	ML.	MR.	NE.	SN.		
		TD,				•	•	•	·	•	•	~,		,		,	,		
US	20042	2148	80		A1		2004	1028	1	US 2	004-	8144	10		2.0	0040	331		
AU	20042	2262									004-					0040			
CA	25193	301																	
	1613										004-								
											IT,								
	•••																SK,	מוז	
ВD	2004	10,	22,	ш.,	шv,	тт,	2006	0411	C1,	AU,	004	0100	C2,	ee,	πυ,	PL,	5K,	пĸ	
CIN	17712	24 / -1 - 2 .	4 -		A.		2006	0210											
	2006				1.7		2006	0525			006-					00404			
PRIORIT	X APEI	∟N	INFO	. :							003-								
										WO 2	004-1	EP34:	98	1	A 20	00404	102		
OTHER S	OURCE	(S):			MAR	PAT	141:	3320	37										

AΒ Title compds. represented by the formula I [wherein R1 = H or alkyl; R2 = (un) substituted (hetero) aryl or heterocyclyl; R1R2 = cyclic hydrocarbon; and pharmaceutically acceptable salts thereof] were prepared as histone deacetylase (HDAC) inhibitors. For example, II was given in a multi-step synthesis starting from the reaction of Me 5-bromomethylthiophene-2carboxylate with 2,3-dihydrobenzo[1,4]dioxine-6-carboxaldehyde oxime. I showed inhibition of HDAC in PC3 cellular acetylation assay with 116-180% control rate. Thus, I and their pharmaceutical compns. are useful as HDAC

10814410.trn

Page 11

06/09/2006

CN

10814410.trn

inhibitors for the treatment of tumor growth (no data).

T 773059-97-5P 773060-02-9P 773060-03-0P

773060-05-2P 773060-08-5P 773060-09-6P

773060-10-9P 773060-11-0P 773060-13-2P

773060-14-3P 773060-15-4P 773060-16-5P

773060-17-6P 773060-18-7P 773060-19-8P

773060-20-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminophenyl thiophenecarboxamide derivs. as HDAC inhibitors for the treatment of tumor growth)

RN 773059-97-5 HCAPLUS

2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(2,3-dihydro-1,4-benzodioxin-6-yl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$NH_2$$
  $O$   $S$   $CH_2-O-N$   $CH$ 

RN 773060-02-9 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(3,4-dichlorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-03-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(phenylmethylene)amino]oxy] methyl]- (9CI) (CA INDEX NAME)

$$Ph-CH=N-O-CH_2$$

$$S$$

$$C-NH$$

RN 773060-05-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(1,3-benzodioxol-5-ylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$NH_2$$
  $CH_2-CH_2-CH_2$ 

RN 773060-08-5 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(4-chlorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-09-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(3,4-dimethoxyphenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-10-9 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(4-fluorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-11-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(2-fluorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-13-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(3-methoxyphenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-14-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(trifluoromethoxy)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$F_3C-O$$
 $CH=N-O-CH_2$ 
 $C-NH$ 

RN 773060-15-4 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(trifluoromethyl)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-16-5 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(diethylamino)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Et}_2\text{N} & \text{O} & \text{H}_2\text{N} \\ \hline \text{CH} & \text{N} - \text{O} - \text{CH}_2 & \text{S} & \text{C} - \text{NH} \\ \end{array}$$

RN 773060-17-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(dibutylamino)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-18-7 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(3-pyridinylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

10814410.trn

Page 14

RN 773060-19-8 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(4-pyridinylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-20-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(2-pyridinylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Imle

=> d ll1 ibib abs hitstr tot

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

5

ACCESSION NUMBER:

2004:857590 HCAPLUS

DOCUMENT NUMBER:

141:332037

TITLE:

Preparation of ammophenyl thiophenecarboxamide

derivatives as HDAC inhibitors for the treatment of

tumor growth

INVENTOR(S):

Fertig, Georg; Herting, Frank; Kubbies, Manfred; Limberg, Anja; Reiff, Ulrike; Weidner, Michael

H. Hoffmann-La Roche Ag, Switz.

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 31 pp.

•

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.			KINI	<b>D</b> 1	DATE		نار ا	APPL:	CAT	ION 1	NO.		D	ATE	
WO 2004		-		A1		2004			viO 2						00404	
W:	AE, A	λG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
	CN, C	co,	CR;	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
	GE, G															
	LK, L															
	NO, N	ΙΖ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,

```
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
               BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
               TD, TG
      US 2004214880
                              A1
                                      20041028
                                                    US 2004-814410
                                                                                20040331
     AU 2004226215
                              A1
                                      20041014
                                                    AU 2004-226215
                                                                                20040402
      CA 2519301
                              AA
                                      20041014
                                                    CA 2004-2519301
                                                                               20040402
      EP 1613622
                              A1
                                      20060111
                                                    EP 2004-725309
                                                                               20040402
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
      BR 2004009182
                              Α
                                      20060411
                                                    BR 2004-9182
                                                                               20040402
      CN 1771247
                              Α
                                      20060510
                                                    CN 2004-80009270
                                                                               20040402
      JP 2006515345
                              T2
                                      20060525
                                                    JP 2006-500084
                                                                               20040402
PRIORITY APPLN. INFO.:
                                                    EP 2003-7829
                                                                            A 20030404
                                                    WO 2004-EP3498
                                                                           A 20040402
                             MARPAT 141:332037
OTHER SOURCE(S):
GΙ
```

Title compds. represented by the formula I [wherein R1 = H or alkyl; R2 = (un)substituted (hetero)aryl or heterocyclyl; R1R2 = cyclic hydrocarbon; and pharmaceutically acceptable salts thereof] were prepared as histone deacetylase (HDAC) inhibitors. For example, II was given in a multi-step synthesis starting from the reaction of Me 5-bromomethylthiophene-2-carboxylate with 2,3-dihydrobenzo[1,4]dioxine-6-carboxaldehyde oxime. I showed inhibition of HDAC in PC3 cellular acetylation assay with 116-180% control rate. Thus, I and their pharmaceutical compns. are useful as HDAC inhibitors for the treatment of tumor growth (no data).

ΙI

IT 773059-97-5P 773059-98-6P 773059-99-7P 773060-00-7P 773060-01-8P 773060-02-9P 773060-03-0P 773060-04-1P 773060-05-2P 773060-06-3P 773060-07-4P 773060-08-5P 773060-09-6P 773060-10-9P 773060-11-0P 773060-12-1P 773060-13-2P 773060-14-3P 773060-15-4P 773060-16-5P 773060-17-6P 773060-18-7P 773060-19-8P 773060-20-1P 773060-21-2P 773060-22-3P 773060-23-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminophenyl thiophenecarboxamide derivs. as HDAC inhibitors for the treatment of tumor growth)

RN 773059-97-5 HCAPLUS

CN

2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(2,3-dihydro-1,4-benzodioxin-6-yl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773059-98-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[1-(4-propylphenyl)ethylidene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\stackrel{\text{N-Pr}}{ } \stackrel{\text{Me}}{ } \stackrel{\text{O}}{ } \stackrel{\text{H}_2\text{N}}{ } \stackrel{\text{O}}{ } \stackrel{\text{$$

RN 773059-99-7 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[1-(2,3-dihydro-2-methyl-4-benzofuranyl)ethylidene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 773060-00-7 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[1-(2,4-dichlorophenyl)ethylidene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} & \text{O} & \text{H}_2\text{N} \\ \hline & \text{C} & \text{N} - \text{O} - \text{CH}_2 & \text{S} & \text{C} - \text{NH} \\ \hline & \text{C}_1 & \text{C}_1 & \text{C}_2 & \text{C}_2 & \text{C}_3 & \text{C}_4 & \text{C}_4 \\ \hline \end{array}$$

RN 773060-01-8 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[1-(3,4-dichlorophenyl)ethylidene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} C1 & & & \\ & Me & & \\ \hline \\ C = N-O-CH_2 & & \\ \end{array}$$

RN 773060-02-9 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(3,4-dichlorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$C1$$
 $CH = N-O-CH_2$ 
 $CH = N-O-CH_2$ 
 $CH = N-O-CH_2$ 

RN 773060-03-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(phenylmethylene)amino]oxy] methyl]- (9CI) (CA INDEX NAME)

RN 773060-04-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(1,3-dihydro-2H-inden-2-ylidene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$N-O-CH_2$$

RN 773060-05-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(1,3-benzodioxol-5-ylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-06-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[1-(3,4-

10814410.trn

Page 19

06/09/2006

10814410.trn

dimethoxyphenyl)ethylidene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-07-4 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(1-phenylethylidene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Ph & O - CH_2 & O & H_2N \\ \hline Me - C - NH & C - NH & C - NH \\ \hline \end{array}$$

RN 773060-08-5 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(4-chlorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-09-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(3,4-dimethoxyphenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-10-9 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(4-fluorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

10814410.trn

Page 20

RN 773060-11-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(2-fluorophenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-12-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[1-(4-fluorophenyl)ethylidene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-13-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[(3-methoxyphenyl)methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-14-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(trifluoromethoxy)phenyl]methylene]amino]oxy]methyl)- (9CI) (CA INDEX NAME)

$$F_3C-O$$
 $CH=N-O-CH_2$ 
 $C-NH$ 

RN 773060-15-4 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(trifluoromethyl)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

F<sub>3</sub>C 
$$CH = N - O - CH_2$$
  $C - NH$ 

10814410.trn

Page 21

RN 773060-16-5 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(diethylamino)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-17-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[[[4-(dibutylamino)phenyl]methylene]amino]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{(n-Bu)}_{2N} \\ \text{CH} \\ \text{=} \text{N-O-CH}_{2} \\ \end{array} \begin{array}{c} \text{S} \\ \text{C-NH} \\ \end{array}$$

RN 773060-18-7 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(3-pyridinylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-19-8 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(4-pyridinylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-20-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(2-pyridinylmethylene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 773060-21-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(1,3-dihydro-2H-inden-2-ylidene)amino]oxy]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

$$N-O-CH_2$$

HCl

RN 773060-22-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(1,3-dihydro-2H-inden-2-ylidene)amino]oxy]methyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 773060-04-1 CMF C21 H19 N3 O2 S

$$N-O-CH_2 \longrightarrow C-NH$$

CM 2

CRN 75-75-2 CMF C H4 O3 S

RN 773060-23-4 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[[[(2,3-dihydro-1H-inden-1-ylidene)amino]oxy]methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

5

```
06/09/2006
```

10814410.trn

=> d his

L5

(FILE 'HOME' ENTERED AT 14:41:12 ON 09 JUN 2006)

FILE 'REGISTRY' ENTERED AT 14:41:24 ON 09 JUN 2006

L1STRUCTURE UPLOADED

0 S L1 L2

L3 16 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 14:41:53 ON 09 JUN 2006

L41 S L3

FILE 'REGISTRY' ENTERED AT 14:42:42 ON 09 JUN 2006

STRUCTURE UPLOADED

L6 0 S L5

L7 27 S L5 SSS FULL

L8 STRUCTURE UPLOADED

 $\hat{L}10$ 

167 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 14:44:28 ON 09 JUN 2006

L111 S L7

L1221 S L10

=> s 112 and py <= 2003

23850918 PY<=2003

11 L12 AND PY<=2003 L13

=> d 113 ibib abs hitstr tot

L13 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:892611 HCAPLUS

DOCUMENT NUMBER:

139:381375

TITLE: Preparation of amides as inhibitors of histone

deacetylase

INVENTOR(S): Stokes, Elaine Sophie Elizabeth; Waring, Michael

James; Gibson, Keith Hopkinson

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.				KIN	D	DATE			APPLICATION NO.					DATE			
					-												
WO 2003092686				A1		20031113		WO 2003-GB1703						20030417 <			
W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	
											MX,						
•	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	
						VC,											
RW:	GH,	GM,	KΕ,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,	
	KG,	ΚZ,	MD,	RU,	TJ,	TM,	AT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	
	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,	
	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
CA 2484				AA		2003			CA 2003-2484065								

AU 2003226553 EP 1501508	A1 20031117 A1 20050202		20030417 < 20030417
R: AT, BE, CH,			L, SE, MC, PT,
IE, SI, LT,			, ,,,
BR 2003009553	A 20050209	BR 2003-9553	20030417
CN 1662236	A 20050831	CN 2003-814828	20030417
JP 2005530748 .	T2 20051013	JP 2004-500870	20030417
NO 2004004557	A 20041022	NO 2004-4557	20041022
US 2005222410	A1 20051006	US 2004-512808	20041026
PRIORITY APPLN. INFO.:		GB 2002-9715	A 20020427
		WO 2003-GB1703	W 20030417
OTHER SOURCE(S):	MARPAT 139:3813	75	

GI

$$\begin{bmatrix} \mathbb{R}^1 \end{bmatrix}_{\mathfrak{m}} \qquad \begin{bmatrix} \mathbb{R}^2 \end{bmatrix}_{\mathfrak{m}} \qquad 0 \qquad \mathbb{R}^4 \end{bmatrix}_{\mathfrak{p}}$$

$$\begin{array}{c|c} & & & \\ & & \\ & & & \\ & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & \\ & & & \\ & & \\ & & & \\ & &$$

AB The title compds. [I; ring A = heterocyclyl; m = 0-4; R1 = OH, halo, CF3, CN; ring B = thienyl, thiadiazolyl, thiazolyl, pyrimidyl, pyrazinyl, pyridazinyl and pyridyl; R2 = halo; n = 0-2; R4 = OH, halo, CF3, CN; p = 0-4; R3 = NH2, OH] or pharmaceutically acceptable salts or in-vivo hydrolysable ester or amide thereof, useful in the treatment of diseases or medical conditions mediated by histone deacetylase such as cancer, were prepared Thus, coupling N-(2-tert-butoxycarbonylaminophenyl)-5bromothiophene-2-carboxamide with pyridine-3-boronic acid in the presence of Pd(PPh3)4 followed by Boc-group removal afforded II. The compds. I showed IC50 of < 2.5  $\mu M$  against recombinant human HDAC1 produced in Hi5 insect cells. The pharmaceutical compns. containing the compound I are claimed.

ΙT 623586-60-7P 623586-61-8P 623586-64-1P 623587-35-9P 623587-36-0P 623587-37-1P 623587-38-2P 623587-39-3P 623587-40-6P 623587-41-7P 623587-42-8P 623587-43-9P 623587-44-0P 623587-45-1P 623587-46-2P 623587-47-3P 623587-48-4P 623587-49-5P 623587-50-8P 623587-51-9P 623587-52-0P 623587-53-1P 623587-54-2P 623587-55-3P

> 623587-56-4P 623587-57-5P 623587-58-6P 623587-59-7P 623587-60-0P 623587-61-1P

623587-62-2P 623587-63-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amides as inhibitors of histone deacetylase)

RN 623586-60-7 HCAPLUS

2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(3-pyridinyl)- (9CI) CN (CA INDEX NAME)

RN623586-61-8 HCAPLUS

2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(4-pyridinyl)- (9CI) (CA CN INDEX NAME)

RN 623586-64-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)

RN623587-35-9 HCAPLUS

2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(1-pyrrolidinyl)- (9CI) (CA CN INDEX NAME)

RN 623587-36-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(1-piperidinyl)- (9CI) (CA INDEX NAME)

RN 623587-37-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 623587-38-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(1,2,3,6-tetrahydro-4-pyridinyl)- (9CI) (CA INDEX NAME)

RN 623587-39-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-(phenylmethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-40-6 HCAPLUS

CN Carbamic acid, [3-[4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]-3,6-dihydro-1(2H)-pyridinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 623587-41-7 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[2-(3,4-dihydro-1(2H)-

10814410.trn

Page 27

quinolinyl)-2-oxoethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 623587-42-8 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-(2-phenoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-43-9 HCAPLUS

CN 1-Piperidinepropanamide, 4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]-N-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & & & \\ \hline PhNH-C-CH_2-CH_2 & & & \\ \hline & N & & & \\ \hline & & C-NH & \\ \hline \end{array}$$

RN 623587-44-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-(3,3-dimethyl-2-oxobutyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-45-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[(3,5-dimethylphenyl)methyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$NH_2 \circ NH_2 \circ$$

RN 623587-46-2 HCAPLUS

CN 1-Piperidinepentanoic acid, 4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]- $\beta$ ,  $\beta$ -dimethyl- $\gamma$ -oxo-, ethyl ester (9CI) (CA INDEX NAME)

RN 623587-47-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[[4-(1,1-dimethylethyl)phenyl]methyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

06/09/2006

10814410.trn

RN 623587-48-4 HCAPLUS

CN 1-Piperidineacetic acid, 4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

RN 623587-49-5 HCAPLUS

CN Benzoic acid, 4-[2-[4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]-1-piperidinyl]ethoxy]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 623587-50-8 HCAPLUS

CN 1-Piperidineacetamide, 4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]-N-(2,6-diethylphenyl)- (9CI) (CA INDEX NAME)

RN 623587-51-9 HCAPLUS

CN 1-Piperidineacetamide, 4-[5-[[(2-aminophenyl)amino]carbonyl]-2-thienyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

06/09/2006

10814410.trn

RN 623587-52-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[(4'-methoxy[1,1'-biphenyl]-4-yl)methyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-53-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-(2,3-dihydroxypropyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

HO- 
$$CH_2$$
-  $CH$ -  $CH_2$ 

N
S
H2N
C-NH

RN 623587-54-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-(4-hydroxybutyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-55-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-(1,2,5-thiadiazol-3-ylmethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-56-4 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[6-(4-hydroxyphenoxy)hexyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-57-5 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[4-(4-hydroxyphenoxy)butyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-58-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[2-(2,4-dimethylphenyl)-2-oxoethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 623587-59-7 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[(5-oxo-2-pyrrolidinyl)methyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-60-0 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[2-(phenylsulfonyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ Ph-S-CH_2-CH_2 \\ O \end{array}$$

RN 623587-61-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[1-[2-([1,1'-biphenyl]-4-yloxy)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

RN 623587-62-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-(1-piperazinyl)- (9CI) (CA INDEX NAME)

RN 623587-63-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

10814410.trn

Page 33

4

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:366795 HCAPLUS

DOCUMENT NUMBER:

138:385301

TITLE:

Preparation of heterocyclyl-substituted

phenylenediamines as p21WAF1 inducers for treatment of

tumor

INVENTOR (S):

Shibata, Tomoyuki; Iwataru, Hayato; Fujiwara, Kosaku

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 30 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003137866 PRIORITY APPLN. INFO.: OTHER SOURCE(S):	A2	20030514	JP 2001-336449 JP 2001-336449	20011101 < 20011101
GI	MARPAT	138:385301		

## \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

2-ArADEGCONHC6H4NH2 [Ar = (un) substituted Q1-Q3, etc.; J, K = bond, CO, CH2; R1 ,R2 = H, C1-6 alkyl, C6-10 aryl; R1R2 may be bonded to form benzene ring; R3R4 = H, R3R4 may be O; R5 = H, C1-6 alkyl; A, E = bond, C1-6 alkylene; D = bond, CO, amido bond; G = C1-6 alkylene, C6-10 arylene, heterocycle residue; A = E ≠ bond; J = K ≠ bond] or their pharmacol. acceptable salts are prepared Thus, Me 4-aminomethylbenzoate HCl salt was amidated with 1,2-dihydrobenzo[cd]indole, hydrolyzed, and condensed with 1,2-phenylenediamine to give 4-(1,2-dihydrobenzo[cd]indol-1-yl)carbonylaminomethyl-N-(2-aminophenyl)benzamide, which induced p21WAF1 with EC50 value of 0.62 μM, vs. 1.90 μM, for MS 275.

IT 524947-02-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclyl-substituted phenylenediamines as p21WAF1 inducers for treatment of tumor)

RN 524947-02-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-5-[(2-oxobenz[cd]indol-1(2H)yl)methyl]- (9CI) (CA INDEX NAME)

```
06/09/2006 10814410.trn
L13 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                               2003:133003 HCAPLUS
DOCUMENT NUMBER:
                                138:175871
TITLE:
                                N-monoacylated derivatives of o-phenylenediamines and
                                their six-membered heterocyclic analogs as antitumor
                                agents
INVENTOR(S):
                                Haag, Rainer; Leser-Reiff, Ulrike; Limberg, Anja;
                                Weidner, Michael; Zimmermann, Gerd
PATENT ASSIGNEE(S):
                                F. Hoffmann-La Roche AG, Switz.
SOURCE:
                                PCT Int. Appl., 27 pp.
                                CODEN: PIXXD2
DOCUMENT TYPE:
                                Patent
LANGUAGE:
                                English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
      PATENT NO.
                              KIND DATE
                                                      APPLICATION NO. DATE
                              ----
                                        -----
                                                       -----
                                                                                     -----
                               A2
      WO 2003013484
                                         20030220 WO 2002-EP8708
                                                                                      20020805 <--
                           A3
      WO 2003013484
                                         20030417
           W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG

                CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
      EP 1416928
                                       20040512 EP 2002-767319
                                A2
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
                            Т2
      JP 2005508311
                                        20050331
                                                       JP 2003-518494
                                                                                      20020805
      US 2003139404
                               A1
                                         20030724
                                                      US 2002-212901
                                                                                      20020806 <--
      US 6869953
                              B2
                                        20050322
      US 2004192744 . A1
                                       20040930
                                                      US 2004-823211
                                                                                      20040413
      US 6946462
                                         20050920
                               B2
                                                        EP 2001-118741
WO 2002-EP8708
PRIORITY APPLN. INFO.:
                                                                               A 20010807
                                                        WO 2002-EP8708
                                                                                 W 20020805
                                                        US 2002-212901 A1 20020806
OTHER SOURCE(S):
                              MARPAT 138:175871
```

Based on the antiproliferative and differentiation-inducing activity, which results in the induction of apoptosis, the title compds. can be used for the treatment of cancer. The compds. were prepared by the reaction of the corresponding carboxylic acid in 0.2M solution of disopropylamine in DMF followed by the addition of 0.1M solution of O-benzotriazol-1-yl-N,N,N',N'tetramethyluronium tetrafluoroborate in DMF and an aryl diamine. Thus, tablets contained the above active compound 5, lactose 125, Sta-Rx 1500 6, microcryst. cellulose 30, and Mg stearate 1 mg/tablet.

497825-25-9P 497825-56-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of monoacylated derivs. of o-phenylenediamines and their 6-membered heterocyclic analogs as antitumor agents)

RN 497825-25-9 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-3-(2-methoxyethoxy)- (9CI) (CA INDEX NAME)

RN 497825-56-6 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-amino-4,5-dichlorophenyl)-3-(2-methoxyethoxy)-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
& & & & C1 \\
& &$$

L13 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:43028 HCAPLUS

DOCUMENT NUMBER: 138:106596

TITLE: Preparation of thiophenedicarboxamides and related

compounds as histone deacetylase (HDAC) inhibitors.

INVENTOR(S): Leser-Reiff, Ulrike; Sattelkau, Tim; Zimmermann, Gerd

PATENT ASSIGNEE(S): Hoffman-La Roche, Inc., Germany

SOURCE: U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	rent	NO.			KIN:	D -	DATE			APPL	ICAT	ION 1	NO.		D	ATE	
	2003 6784		_		A1 B2		2003 2004			US 2	002-	1676	77		2	0020	611 <- <b>-</b>
CA	2449 -2003	804			AA		2003 2003	0213		CA 2 WO 2							613 < 613 <
	2003											DI () I	00		. 24	0020	013 <
	<b>W</b> :	ΑĒ,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
										EC,							
										KΕ,							
										MN,							
										SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
							ZA,										
	RW:	GH,	GM,	KΕ,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	CH,	CY,	DE,	DK,	ES,	FI,	FR,	GB,
		GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
		GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG							
ΕP	1401																
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,

IE, SI, LT,	LV,	FI, RO, MK,	CY, AL, TR		
CN 1516697	A	20040728	CN 2002-812010		20020613
BR 2002010424	Α	20040817	BR 2002-10424		20020613
NZ 529874	A	20041224	NZ 2002-529874		20020613
JP 2005502641	T2	20050127	JP 2003-517043		20020613
ZA 2003009260	Α	20050228	ZA 2003-9260		20031127
BG 108450	Α	20050131	BG 2003-108450		20031215
US 2004214862	A1	20041028	US 2004-847166		20040517
PRIORITY APPLN. INFO.:			EP 2001-114496	Α	20010615
			US 2002-167677	A3	20020611
,			WO 2002-EP6488	W	20020613

OTHER SOURCE(S): MARPAT 138:106596

HONHCOACONR1R2 [A = (substituted) Ph, thienyl; R1, R2 = H, (substituted) AΒ alkyl, carbocyclyl, heterocyclyl; NR1R2 = (substituted) 3-6 membered ring], were prepared Thus, thiophene-2,5-dicarboxylic acid monomethyl ester and N-methylmorpholine in CH2Cl2 at -10° were treated with 1-aminomethylnaphthalene in CH2Cl2; the mixture was stirred 90 min to give 58% monoamide. This was stirred with NH2OH.HCl and NaOMe in MeOH for 4 h to give thiophene-2,5-dicarboxylic acid 2-hydroxyamide 5-[(naphthalen-1-ylmethyl)amide]. Tested title compds. inhibited HT-29 tumor cell growth with IC50 =  $0.02-0.17~\mu M$ . A tablet formulation is given.

## 487004-93-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(claimed compound; preparation of thiophenedicarboxamides and related compds.

as histone deacetylase (HDAC) inhibitors)

RN 487004-93-3 HCAPLUS

CN 2,5-Thiophenedicarboxamide, N-(2-aminophenyl)-N'-hydroxy- (9CI) (CA INDEX NAME)

$$HO-NH-C$$

$$S$$

$$C$$

$$NH$$

$$C$$

$$NH$$

REFERENCE COUNT: THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS 9 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:228885 HCAPLUS

DOCUMENT NUMBER:

134:252339

TITLE:

Preparation of benzimidazole derivatives as poly(ADP-ribose) polymerase (PARP) inhibitors

INVENTOR (S):

Takayama, Kazuhisa; Koga, Yuji; Masuda, Naoyuki;

Miyazaki, Yoji; Kimura, Takenori; Nagashima, Shinya; Okamoto, Yoshinori; Okada, Yohei; Takeuchi, Makoto

PATENT ASSIGNEE(S):

Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE:

PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

GI

PATENT NO	٥.	•	KINI	) 1	DATE		i	APPL:	I CAT	ION	NO.		D2	ATE	
						<b></b> -									
WO 200102	21615		A1	2	2001	0329	1	WO 2	000-	JP63	19		20	0000	914 <
W: A	AE, AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
	CR, CU,														
I	HU, ID,	ΙL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,
]	LU, LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	NZ,	PL,	PT,	RO,	RU,
	SD, SE,														
7	YU, ZA,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM				
RW: 0	GH, GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	ΒE,	CH,	CY,
I	DE, DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,
(	CF, CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
PRIORITY APPL	N. INFO	:						JP 19	999-2	26443	31	1	19	9990	917
							,	JP 20	000-	1707	15	1	A 20	00006	507
OTHER SOURCE (S	S):		MARE	PAT 1	134:2	2523	39								

- Benzimidazole derivs. having heterocyclic groups at the 2-position and carbamoyl at the 4-position as represented by general formula (I) or (II) or salts thereof (wherein R1 is H, lower alkyl, halo, or halo-lower alkyl; R2 is H, lower alkyl, or lower alkyl-carbonyl; and A is an optionally substituted heterocyclic group), which are useful in the prevention or the treatment of various PARP-related diseases such as inflammations (in particular chronic articular rheumatism), autoimmune diseases, and ischemic reperfusion disorders, are prepared Thus, 3.58 g Me 2-(pyridin-4-yl)-1H-benzimidazole-4-carboxylate was added to 35 mL NH4(1) at -50° in a metal sealed tube and heated at 140° for 3 days to give 2.58 g 2-(pyridin-4-yl)-1H-benzimidazole-4-carboxamide (III). III and 15 other compds. of I and II in vitro showed IC50 of 7-50 nM against PARP.
- IT 330947-91-6P, 2-Amino-3-[(thiophene-2-carbonyl)amino]benzoic acid methyl ester

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzimidazole derivs. as poly(ADP-ribose) polymerase (PARP) inhibitors in prevention or treatment of various PARP-related diseases) 330947-91-6 HCAPLUS

CN Benzoic acid, 2-amino-3-[(2-thienylcarbonyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

RN

Ι

REFERENCE COUNT:

12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2000:769086 HCAPLUS

DOCUMENT NUMBER:

133:335159

TITLE:

Preparation of N-pyridinyl-2-

[(thienylcarbonyl)amino]benzamides and analogs as

anticoaqulants

INVENTOR(S):

Arnaiz, Damian O.; Chou, Yuo-ling; Griedel, Brian D.; Karanjawala, Rushad E.; Kochanny, Monica J.; Lee, Wheeseong; Liang, Amy Mei; Morrissey, Michael M.; Phillips, Gary B.; Sacchi, Karna Lyn; Sakata, Steven T.; Shaw, Kenneth J.; Snider, R. Michael; Wu, Shung

C.; Ye, Bin; Zhao, Zuchun

PATENT ASSIGNEE(S):

Berlex Laboratories, Inc., USA

SOURCE:

U.S., 113 pp., Cont.-in-part of U.S. Ser. No. 994,284,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		APPLICATION NO.	DATE
US 6140351	A 20001031	US 1998-187459	19981105 <
CA 2315070	AA 19990701	CA 1998-2315070	19981127 <
		WO 1998-EP7650	
		BG, BR, BY, CA, CH, CN	
DK. EE. ES	. FI. GB. GE. GH.	GM, HR, HU, ID, IL, IS	TP KE KG
		LT, LU, LV, MD, MG, MK	
		SE, SG, SI, SK, SL, TJ	
	, 11, KO, KO, DD, , VN, YU, ZW	55, 56, 51, 5K, 5E, 10	, IM, IK, II,
		UG, ZW, AT, BE, CH, CY	DE DY EG
		MC, NL, PT, SE, BF, BJ	, CF, CG, C1,
	, GW, ML, MR, NE,		
		AU 1999-18759	19981127 <
AU 751856			
		EP 1998-963519	19981127 <
	B1 20040225		
R: AT, BE, CH	, DE, DK, ES, FR,	GB, GR, IT, LI, LU, NL	, SE, MC, PT,
IE, FI			
JP 2001526283	T2 20011218	JP 2000-525414	19981127 <
NZ 503809	A 20020426	NZ 1998-503809	19981127 <
AT 260103	E 20040315	AT 1998-963519	19981127
RU 2226529	C2 20040410		
PT 1040108		PT 1998-963519	
ES 2215337		ES 1998-963519	
	A 19990817		
	1000017		19901211 <

NO 2000003111	Α	20000818	NO	2000-3111		20000616 <
US 6380221	B1	20020430	US	2000-631450		20000803 <
US 6498185	В1	20021224	US	2000-631452		20000803 <
PRIORITY APPLN. INFO.:			US	1997-994284	B2	19971219
			US	1998-187459	A	19981105
			WO	1998-EP7650	W	19981127

OTHER SOURCE(S):

MARPAT 133:335159

GI

AB REZDR3 [I; D,E = Z1NR5C(:X), Z1NR5SO0-2, etc.; R,R3 = (un)substituted heterocyclyl or -aryl; R5 = H, (ar)alkyl, aryl; X = O, S, H2; Z = (un)substituted heterocyclylene or -arylene; Z1 = bond, alkylene, alkylidene, etc.] were prepared as factor Xa, thrombin, and prothrombinase inhibitors. Thus, H2NZCONHC6H4Cl-4 (Z = 4-chloro-1,2-phenylene) (preparation given) was N-acylated by 3-chloro-4-chloromethyl-2-thiophenecarbonyl chloride and the product aminated by 1-methylpiperazine to give title compound II. Data for biol. activity of I were given.

IT 229343-40-2P

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-pyridinyl-2-[(thienylcarbonyl)amino]benzamides and analogs as anticoagulants)

RN 229343-40-2 HCAPLUS

2-Thiophenecarboxamide, N-[2-amino-4-chloro-6-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]-3-chloro-4-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

IT 229342-73-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-pyridinyl-2-[(thienylcarbonyl)amino]benzamides and analogs as anticoagulants)

RN 229342-73-8 HCAPLUS

CN 2-Thiophenecarboxamide, N-[2-amino-4-chloro-6-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]-3-chloro-4-(chloromethyl)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

1999:421679 HCAPLUS

DOCUMENT NUMBER:

131:87925

TITLE:

Preparation of heteroarylcarbonylaminobenzamides and

related compounds as anticoagulants.

INVENTOR(S):

Arnaiz, Damian O.; Chou, Yuo-Ling; Karanjawala, Rushad E.; Kochanny, Monica J.; Lee, Wheeseong; Liang, Amy Mei; Morrissey, Michael M.; Phillips, Gary B.; Sacchi, Karna Lyn; Sakata, Stephen T.; Shaw, Kenneth J.;

Karna Lyn; Sakata, Stephen T.; Shaw, Kenneth J.; Snider, R. Michael; Wu, Shung C.; Ye, Bin; Zhao,

Zuchun; Griedel, Brian D.

PATENT ASSIGNEE(S):

Schering Aktiengesellschaft, Germany

10814410.trn

Page 41

14:47

06/09/2006

10814410.trn

SOURCE:

PCT Int. Appl., 326 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

٠. ٦

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	TENT															ATE		
	9932	477			A1		1999	0701		WO 1		EP76	50		1			
	W :						, BA,											
							GE,											
		ΚP,	KR,	ΚZ,	LC,	LK	, LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	
		NO,	NZ,	PL,	PT,	RO.	, RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	
		UA,	UG,	UZ,	VN,	YU,	, ZW											
	RW:	GH,	GM,	ΚE,	LS,	MW	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,	
		FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	
							MR,										•	
US	6140	351			Α		2000	1031		US 1	998-	1874	59		1	9981	105	<
	2315				AA		1999	0701	•	CA 1	998-:	2315	070		1	9981	127	<
AU	9918	759			A1		1999	0712		AU 1	999-	1875	9		1	9981	127	<
AU	7518	56			B2		2002	0829										
	1040									EP 1	998-	9635	19		1	9981	127	<
EP	1040	108			B1		2004	0225										
	R:	AT,	BE,	CH,	DΕ,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,									-	-	,	•		•	•	
	2001						2001	1218		JP 2	000-	5254	14		1:	9981	127	<
NZ	5038	09			Α		2002	0426		NZ 1	998-	5038	09		1:	9981	127	<
AT	2601	03			E		2004	0315			998-							
RU	2226	529			C2		2004	0410										
NO	2000	0031	11		Α		2000				000-3					0000		
PRIORITY										US 1	997-	9942	84	1		9971		
										US 1	998-	1874	59	1	A 1	9981	105	
											998-1							
OTHER SO					MAR	PAT	131:	8792										

$$(R^1)_{\mathfrak{m}}$$
  $EQ(R^4)_{\mathfrak{n}}$   $B$   $P^2$   $DR^3$   $I$ 

Title compds. [I; m = 1-3; n = 1-5; B, Q = atoms to form aryl, heterocyclyl rings; D, E = NR5CX; R8NR5CX, NR5SOp, etc.; p = 0-2; X = 0, S, H2; R1 = H, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, OR5, CO2R5, NR5R6, CONR5R6 (substituted) heterocyclyl, etc.; R2 = H, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, OR5, CO2R5, CONR5R6, etc.; R3 = (substituted) heterocyclyl, aryl; R4 = H, alkyl, halo, haloalkyl, cyano, NO2, OR5, CO2R5, NR5R6, etc.; R5, R6 = H, alkyl, aryl, aralkyl; R8 = alkylene, alkenylene, alkynylene], were prepared Thus, N-(4-chlorophenyl)-2-[[(4-chloromethyl)-3-chlorothiophen-2-ylcarbonyl]amino]-3-methoxy-5-chlorobenzamide in DMF at 0° was treated with N-methylpiperazine followed by stirring to room temperature to give N-(4-chlorophenyl)-2-[[[4-[(4-methylpiperazin-1-yl)methyl]-3-chlorothiophen-2-yl]carbonyl]amino]-3-

methoxy-5-chlorobenzamide. Title compds. routinely inhibited Factor Xa with Ki<3 nM. An aerosol formulation is given.

IT 229342-73-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of heteroarylcarbonylaminobenzamides and related compds. as anticoagulants)

RN 229342-73-8 HCAPLUS

CN 2-Thiophenecarboxamide, N-[2-amino-4-chloro-6-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]-3-chloro-4-(chloromethyl)- (9CI) (CA INDEX NAME)

IT 229343-40-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heteroarylcarbonylaminobenzamides and related compds. as anticoagulants)

RN 229343-40-2 HCAPLUS

CN 2-Thiophenecarboxamide, N-[2-amino-4-chloro-6-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]-3-chloro-4-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10814410.trn

Page 43

2

14:47

L13 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:207259 HCAPLUS

DOCUMENT NUMBER: 114:207259

TITLE: Preparation of benzothiazoles and benzimidazoles as

blood platelet aggregation inhibitors

INVENTOR(S): Nishi, Takao; Uno, Tetsuyuki; Koga, Yasuo; Shu,

Yoshio; Igawa, Takehiro

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 71 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02306916	A2	19901220	JP 1989-128245	19890522 <
JP 2869561	B2	19990310		
PRIORITY APPLN. INFO.:			JP 1989-128245	19890522
OTHER SOURCE(S):	MARPAT	114:207259		
GI				

$$(R^1)_n \xrightarrow{N}_{R^2 - I} C1 \xrightarrow{N}_{S} \xrightarrow{N}_{R - II}$$

AB The title compds. [I; R1 = halo, cyano, cyanoalkoxy, (substituted) alkyl, acyl, etc.; R2 = alkyl-substituted pyrrolyl, thienyl, pyridylthioalkyl, halophenyl, etc.; X = NR3; R3 = H, alkyl, alkenyl, phenylalkyl; n = 0-2] were prepared Heating a mixture of 1 g dichloro compound II (R = Cl) and 4.2 g piperazine in  $\alpha$ -picoline at 100° gave 0.31 g II.HCl (R = piperazino), that gave 78.95% blood platelet aggregation inhibition at 1 + 10-4 mol. Among 178 addnl. I prepared, 60 tested effective. Tablet, capsule, and injection formulations were given.

IT 133687-95-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of blood platelet aggregation inhibitor)

RN 133687-95-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-amino-4-nitrophenyl)- (9CI) (CA INDEX NAME)

L13 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

10814410.trn

Page 44

14:47

ACCESSION NUMBER: 1987:18589 HCAPLUS

DOCUMENT NUMBER: 106:18589

TITLE: Pyridazinones, their use as cardiovascular agents and

their formulations

INVENTOR(S): Hauel, Norbert; Narr, Berthold; Noll, Klaus; Bomhard,

Andreas; Heider, Joachim; Psiorz, Manfred; Diederen, Willi; Van Meel, Jacques

PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.

Ger. Offen., 40 pp. SOURCE:

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: D3 mmim 310

PA	TENT NO.	KIND	DATE	APPLICATION NO.		DATE	
					<del>-</del> -		
DE	3511110	A1	19861002	DE 1985-3511110		19850327	<
EP	196005	A1	19861001	EP 1986-103687		19860318	<
EP	196005	B1	19891220				
	R: AT, BE, CH,	DE, FR	, GB, IT,	LI, LU, NL, SE			
AT	48841	E	19900115	AT 1986-103687		19860318	<
DK	8601318	A	19860928	DK 1986-1318		19860321	<
DD	248362	A5	19870805	DD 1986-288285	•	19860325	<
CA	1257588	A1	19890718	CA 1986-505012		19860325	<
FI	8601288	A	19860928	FI 1986-1288		19860326	
NO	8601266	A	19860929	NO 1986-1266		19860326	<
AU	8655303	A1	19861002	AU 1986-55303		19860326	
JP	61227582	A2	19861009	JP 1986-68255		19860326	<
ES	553463	A1	19870516	ES 1986-553463		19860326	<
HU	42085	A2	19870629	HU 1986-1275		19860326	<
ZA	8602248	A	19871125	ZA 1986-2248		19860326	<
ES	557218	A1	19870516	ES 1986-557218		19861121	
ES	557219	A1	19870516	ES 1986-557219		19861121	<
ES	557220	A1	19870516	ES 1986-557220		19861121	<
PRIORITY	Y APPLN. INFO.:			DE 1985-3511110	Α		
				EP 1986-103687	A	19860318	
OTHER SO	OURCE(S):	CASREA	CT 106:185	589; MARPAT 106:18589			
~-							

Title compds. I (X = NR3, O, S; R1 = N-containing heterocyclyl; R2 = H, alkyl; AB R3 = H, alkyl, Ph), useful for treatment of angina, heart failure, high blood pressure, and for prophylaxis of thromboembolisms, were prepared Benzoxazolylpyridazinone II (R4 = SMe) reacted with imidazole to give 31.4% II (R4 = imidazol-1-yl) (III). In cats 0.1 mg III/kg i.v. decreasesd blood pressure 43-45 mm Hg. Tablets were prepared each containing III 50.0, lactose 40.0, corn starch 17.0, polyvinylpyrrolidone 2.0, Mg stearate 1.0 mg.

ΙT 105737-18-6

GI

II

> RL: RCT (Reactant); RACT (Reactant or reagent) (cyclization of, benzimidazole by)

RN 105737-18-6 HCAPLUS

2-Thiophenecarboxamide, N-[2-amino-4-(1,4,5,6-tetrahydro-6-oxo-3-CN pyridazinyl)phenyl] - (9CI) (CA INDEX NAME)

L13 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

1981:115825 HCAPLUS

DOCUMENT NUMBER:

94:115825

TITLE:

Thiophene carboxamide fungicides: structure-activity relationships with the succinate dehydrogenase complex from wild-type and carboxin-resistant mutant strains

of Ustilago maydis

AUTHOR (S):

White, G. A.; Thorn, G. D.

CORPORATE SOURCE:

Res. Inst., Agric. Canada, London, ON, N6A 5B7, Can.

SOURCE: Pesticide Biochemistry and Physiology (1980

), 14(1), 26-40

CODEN: PCBPBS; ISSN: 0048-3575

DOCUMENT TYPE: Journal

LANGUAGE:

English

A variety of thiophene carboxamide compds. were synthesized and tested on the succinate dehydrogenase [9002-02-2] complex (SDC) in mitochondria from a wild-type strain and carboxin (I) [5234-68-4]-resistant strains of U. maydis (corn smut). The action site of thiophene carboxamides is identical to that of I and thenoyltrifluoroacetone, i.e., the succinate-ubiquinone reductase (complex II) span in the mitochondrial electron transfer chain. This investigation reveals new mol. structures which are strong inhibitors of wildtype and I-resistant SDCs. The 5-amino analog of the parent anilide 3-methylthiophene-2-carboxanilide (II) [56776-44-4] proved to be an especially potent inhibitor of the wild-type SDC (I50, 0.019  $\mu M)$  . Analogs of II such as the 4'-carboethoxy [76656-08-1], 4-butyl [76656-09-2], 4-phenyl [76656-10-5], and 4'-benzoyl [76656-11-6] derivs. were neg. correlated in activity to II with respect to resistance level. A number of structures showed considerable selectivity for mutated SDCs from both highly and (particularly) moderately I-resistant SDCs of U. maydis, markedly lowering the resistance level, i.e., the degree of resistance. Thus, in addition to the oxathiins, specific structural groups of thiophene carboxamide can also alleviate or reverse the effect of I-selected mutation with reference to inhibition of the SDC. Mol. selectivity for mutated, I-resistant SDCs can be influenced by replacement of an oxathiin by a thiophene heterocyclic ring as well as by the substitutive group on the amide N, permitting different categories of mutant types and even mutants within a single category to be distinguished from one another. With all the structural combinations available, it appears quite possible, in terms of inhibition, to overcome any type of mutation in a fungal SDC which arises through selection by I or other carboxamide compds. A correlation generally exists between resistant strains of U. maydis. A permeability barrier to 4'-substituted analogs of II was encountered in the wild-type strain, but not mutant strains.

Excellent protectant activity against bean rust (Uromyces phaseoli) was obtained with 3'-hexyl [76656-12-7], 3'-hexyloxy [76656-13-8], and 4'-phenoxy [76656-14-9] analogs of II.

IT 76655-79-3

RL: BIOL (Biological study)

(succinate dehydrogenase complex of Ustilago maydis wild-type and carboxin-resistant strains in response to)

RN 76655-79-3 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-3-methyl- (9CI) (CA INDEX NAME)

L13 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

1973:492218 HCAPLUS

DOCUMENT NUMBER:

79:92218

TITLE:

Fungicidal 2-(2-thienyl)benzimidazoles

INVENTOR(S):

Meyer, Friedrich J.; Kaspers, Helmut; Scheinpflug,

Hans

PATENT ASSIGNEE(S):

Bayer A.-G.

SOURCE:

Ger. Offen., 22 pp.

CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2201062	A1	19730726	DE 1972-2201062	19720111 <
US 3810910	A	19740514	US 1972-318964	19721227 <
NL 7300255	. <b>A</b>	19730713	NL 1973-255	19730108 <
CH 548415	A	19740430	CH 1973-241	19730109 <
IT 978066	Α	19740920	IT 1973-19102	19730109 <
GB 1364218	A	19740821	GB 1973-1271	19730110 <
FR 2167954	A1	19730824	FR 1973-888	19730111 <
JP 48080559	A2	19731029	JP 1973-5567	19730111 <
JP 48080736	A2	19731029	JP 1973-5568	19730111 <
PRIORITY APPLN. INFO.:			DE 1972-2201062 A	19720111

GI For diagram(s), see printed CA Issue.

AB Seven benzimidazoles (I, R = Me, Et, CHMe2, or Bu; R1 = H or Br) were prepared by reaction of II with ClCO2R and used as fungicides. Thus, 175 g o-phenylenediamine 117 g thiophene-2-carbonyl chloride and CH2Cl was stirred 18 hr at room temperature to give 44.5%

N-(2-thenoyl)-o-phenylenediamine-

HCl, which was heated with POCl3 at 75-92° for 3 hr to give 82% 2-(2-thienyl)benzimidazole (II; R1 = H), which was treated with ClCO2Me 16 hr to give 88.4% I (R1 = H, R = Me).

IT 49542-28-1P

RN 49542-28-1 HCAPLUS

CN 2-Thiophenecarboxamide, N-(2-aminophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

=> log y		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	76.55	580.55
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-9.75	-9.75

STN INTERNATIONAL LOGOFF AT 14:47:05 ON 09 JUN 2006